REMARKS

Claims 10-24 are pending. Claims 10, 11, 13-17, and 20-22 have been amended and claims 25 and 26 have been added. Therefore, claims 10-26 are pending in the application.

Support for these amendments can be found throughout the specification, including at page 1, lines 14-16 and page 2, lines 11-12 and 18-21. These amendments introduce no new matter.

Rejections under 35 U.S.C. 112, Second Paragraph

Claims 10-24 are rejected as being indefinite. According to the Action, there is "insufficient antecedent basis" for the following terms in the claims listed below:

"said inflammation or pain" in claim 10;

"the spinal vertabrae" in claim 11;

"the calcium salt" in claim 13;

"the injectable medicament" in claim 14; and

"the medicament" in claims 20-22.

Applicants submit that the rejections no longer apply to claims 10, 11, 13, 14, and 20-22 as amended and respectfully request that these rejections be withdrawn. Applicants further submit that the rejection of dependent claims 12, 15-19, 23, and 24 be withdrawn as they no longer depend upon an indefinite base claim.

Rejection under 35 U.S.C. 102(b)

Claims 10-15 and 20 are rejected as being anticipated by Hyodo et al., U.S. Patent 5,260,289 (Hyodo). According to the Action, "Hyodo et al. teach a method of using a composition comprising NEO VITACAIN™, which comprises 100 mg/100ml of calcium pantothenate and 100 mg/100ml of dibucaine hydrochloride (a local anesthetic), for the local treatment of pain" (Action, page 3, lines 9-11).

Applicants' invention is based on the discovery that "pantothenic acid is of value in reducing inflammation when injected into the region of an affected joint" (Specification, page 1, lines 12-13).

Hyodo discloses and claims a method for alleviating pain that includes "injecting a composition containing dibucaine, a pharmaceutically acceptable salt of salicylic acid, calcium bromide, and antiphlogistic steroid" (Hyodo, col. 2, lines 18-21). The subjects being treated by the claimed method are administered with a composition containing the antiphlogistic steroid and "Neo Vitacain," (Hyodo, col. 3, lines 19-21 and col. 5, line 50 through col. 7, line 6). According to Hyodo, Neo Vitacain is a known analgesic having a formulation containing "dibucaine hydrochloride, sodium salicylate, and calcium bromide as 'active ingredients' for use in a pain treatment," along with "thiamine HCl," "pyridoxin HCl," and "calcium pantothenate" (Hyodo, col. 1, lines 28-49, emphasis added). Since calcium pantothenante is not listed among the "active ingredients" in Neo Vitacain, Hyodo provides no basis to conclude that calcium pantothenate possesses analgesic properties or would be an active agent for the treatment of pain. Moreover, there is no indication in Hyodo that calcium pantothenate is useful for treating inflammation.

Applicants recite below the holdings from *In re Hoeksema* and *In re Donohue* regarding the general level of operability required to make a *prima facie* case of anticipation:

> In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure' *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968).

> A reference contains an 'enabling disclosure' if the public was in possession of the claimed invention before the date of invention. 'Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention' (In re Donohue, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985).

The case law cited above makes clear that the anticipatory reference must enable the invention that it allegedly anticipates. Hyodo teaches a method of treating pain using a composition having, at a minimum, dibucaine, a pharmaceutically acceptable salt of salicylic acid, calcium bromide, and an antiphlogistic steroid, but does not provide any indication that calcium pantothenate in the absence of the "active ingredients" can be used in methods of treating inflammation or pain. Hyodo provides no teaching that calcium pantothenate has any role whatsoever in treating pain, and effectively indicates that calcium pantothenate is an inactive component of the analgesic Neo Vitacain. In short, Hyodo does not teach one of skill in the art how to treat pain or inflammation using calcium pantothenate and therefore does not enable Applicants' claimed method. Applicants therefore respectfully request that the rejection of claims 10-15 and 20 be withdrawn on the grounds that the prior art reference Hyodo is not an disclosure of Applicants' claimed method.

Rejections under 35 U.S.C. 103(a)

Claims 10-16 and 20-21 are rejected as being unpatentable over Hyodo, as applied to claims 10-15 and 20 above and further in view of UK Patent Number 1,145,623 (the '623 Patent).

Hyodo discloses and claims a method for alleviating pain that includes the local administration of a composition containing dibucaine, a pharmaceutically acceptable salt of salicylic acid, calcium bromide, and antiphlogistic steroid. Hyodo states that an object of the invention "is to provide a novel use of antiphlogistic steroids as contained in a composition for reinforcing pain relief action, which is used with other analgesics such as Neo Vitacain injection for the treatment of pain" (Hyodo, col. 1, lines 57-61). As discussed above, "Neo Vitacain," contains "dibucaine hydrochloride, sodium salicylate, and calcium bromide as 'active ingredients' for use in a pain treatment," along with "thiamine HCl," "pyridoxin HCl," and "calcium pantothenate" (Hyodo, col. 1, lines 28-49, emphasis added).

Applicants submit that calcium pantothenate is disclosed essentially by happenstance in Hyodo, as merely being part of the Neo Vitacain formulation. There is no teaching or suggestion

in Hyodo that calcium pantothenate plays any role in the treatment of pain, regardless of whether Neo Vitacain is administered alone or in combination with the antiphlogistic steroids. Further there is no teaching in Hyodo that would motivate one of skill in the art to select calcium pantothenate from the list of formulation ingredients (Hyodo, col. 1, lines 40-50 and col. 5, lines 23-43) and test it for effectiveness in pain treatment by local administration. Again, Hyodo discloses compositions that require dibucaine hydrochloride, sodium salicylate and calcium bromide, administered along with an antiphlogistic steroid. It would therefore not have been obvious to one of ordinary skill to try to treat pain by local administration of calcium pantothenate in the absence of Neo Vitacain and the antiphlogistic steroid on the basis of the Hyodo disclosure.

The '623 Patent discloses compositions containing *d*-pantothenic acid, or physiologically acceptable salts thereof, and cysteine or cystine. These compositions are described to be useful for the alleviation of arthritis. According to the '623 Patent specification, the compositions may be adapted for oral, parenteral or rectal administration ('623 Patent, page 1, lines 74 and 82 and page 2, line 18). In other words, the '623 Patent teaches only <u>systemic</u> treatment of arthritis using the combination of d-pantothenic acid (or salts thereof) and cysteine or cystine. Moreover, only oral administration is exemplified..

Hyodo teaches <u>local</u> administration of compositions containing dibucaine, a pharmaceutically acceptable salt of salicylic acid, calcium bromide, and antiphlogistic steroid. According to the Specification, "the aforementioned compositions are preferably injected into the location site of pain,...such as into muscle, peritenon and articular activity" (Hyodo, col. 3, lines 47-49 and col. 4, lines 5-6). As discussed above, Hyodo fails to provide any teaching or suggestion that local administration of calcium pantothenate results in the relief of pain. Hyodo exemplifies local administration only. Therefore, one of skill in the art would not be motivated to modify the local method of Hyodo to include the systemic compositions of the '623 Patent because the compositions demonstrated to have pain relief activity in Hyodo (i.e., the composition containing dibucaine, a pharmaceutically acceptable salt of salicylic acid, calcium bromide, and antiphlogistic steroid) are distinct and different (structurally, functionall, and local

v. systemic) from those compounds demonstrated to have pain relief activity in the '623 Patent (i.e., d-pantothenic acid or physiologically acceptable salts and cysteine or cystine). Furthermore, neither Hyodo or the '623 Patent discuss treatment of inflammation.

Based on the foregoing, Applicants respectfully request withdrawal of the rejection of claims 10-16 and 20-21 on the grounds that there is a lack of motivation to combine Hyodo and the '623 Patent to arrive at the claimed invention.

Claims 10-24 are rejected as being unpatentable over Hyodo et al. taken with UK Patent Number 1,145,623, as applied to claims 10-16 and 20-21 and further in view of Rozenburg, RU 2078564C1 (Abstract only; Rozenburg).

Rozenburg discloses that "Aseptic inflammations can be treated more effectively by administering glucocorticoids...by administering them in a liposome membrane. The liposomal composition...consists of (wt.%): dipalmitoyl phosphatidylcholine [DPPC] (1.6-2.0); cholesterol (0.20-0.25)" (Rozenburg). Rozenburg discloses that DPPC is a useful adjunct for improving the effectiveness of glucocorticoids in the treatment of septic inflammations *vis a vis* as a liposomic carrier for the active component used in Rozenburg. On the other hand, Applicants' Specification states "surface active phospholipid (SAPL) such as dipalmitoyl phosphatidylcholine (DPPC)...are believed to act as a lubricant in joints, taking over to some extent the function of sinovial fluid" (Specification, page 2, lines 9 and 13-14). Thus, the intended function of DPPC in Applicants' claimed method is distinct and different from that disclosed in Rozenburg. Therefore, one of skill in the art are would not be motivated to combine the teachings of Rozenburg, with those of the '623 Patent and Hyodo to arrive at Applicants' claimed method.

Applicants respectfully request that the rejection of claims 10-24 over Hyodo taken with the '623 Patent and in view of Rozenburg be withdrawn for the reasons set forth above.

No fee is believed due with this response. Please apply any charges to deposit account 06-1050, referencing Attorney Docket No. 13596-003US1.

Respectfully submitted,

Date: November 3, 2003

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